

A polynucleotide is provided which comprises at least two repeats of a hypoxia element (HRE), wherein the hypoxia-inducible factor consensus binding sites within each of the two repeats are separated by a spacer of at least 20 contiguous nucleotides. A

two repeats are separated by a spacer of at least 20 contiguous nucleotides. The polynucleotide is also provides which comprised at least three repeats of a phosphoglycerate kinase (PGK) hypoxia response element (HRE) operably linked to an SV40 promoter or an MLV promoter. The polynucleotide may be operably linked to a nucleic acid of interest to drive expression of the NOI in a cell under hypoxic conditions.

Year	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
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